Remarks

Objection to the Claims

The Office Action objected to claims 92 and 94 because they contain a typographical error. This amendment corrects the error.

Rejection Under 35 U.S.C. § 112 ¶ 1

Claims 69 and 92-94 are rejected under 35 U.S.C. § 112 ¶ 1 as not enabled. Applicants respectfully traverse the rejection.

The enablement requirement of 35 U.S.C. § 112 ¶ 1 states that a patent specification must teach a person skilled in the relevant art how to make and use the invention claimed. Whether a specification enables a claimed invention is a question of law based on underlying factual findings. *In re Vaeck*, 947 F.2d 488, 495, 20 U.S.P.Q.2d 1438, 1444 (Fed. Cir. 1991). The proper standard for determining whether the present specification meets the enablement requirement is whether any experimentation which may be needed to practice the methods of claims 69 and 92-94 is undue or unreasonable. *In re Wands*, 858 F.2d 731, 736-37, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988).

Claims 69 and 92-94 are directed to methods for inhibiting tumor cell growth in an animal. The methods comprise administering to the animal an effective amount of a composition which consists essentially of a hemagglutinating virus of Japan envelope (HVJ-E). The Examiner has the initial burden to establish a reasonable basis to question why the specification does not enable the claimed methods. *In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993). The Examiner must not only explain why she doubts the statements in the specification's supporting disclosure, but also must support her assertions "with acceptable evidence or reasoning which is inconsistent with the contested statement." *In re Marzocchi*, 439 F.2d 220, 224 (C.C.P.A. 1971). Thus, a proper

enablement rejection should contain specific findings of fact—supported by evidence—and conclusions based on those findings of fact. See M.P.E.P. § 2164.04.

The Examiner acknowledges that the HVJ-E vector "has adjuvant properties for enhancing an anti-tumor response" but asserts that "those adjuvant properties alone are not expected by one of skill in the art to have any anti-tumor cell growth without the accompanying chemotherapeutic agent." Office Action at page 4 ¶ 1. The rejection does not contain any specific findings of fact or evidence to support this assertion and does not make a *prima facie* case that claims 69 and 92-94 are not enabled.

First, the Examiner ignores the enabling teachings in the specification itself. In the Examples of the specification, the results of Study 1 demonstrate that administration of HVJ-E inhibits growth of tumor cells, as evidenced by the tumor volume of 82.9% in the HVJ-E group as compared to the control group (paragraph [0214]) and Fig. 1, showing the volume. In addition, the results of Example 5 reveal that an increase in the tumor volume can be inhibited even in the HVJ-E alone group (paragraph [0276], Fig. 16 and Fig. 17, particularly Fig. 17). Example 5 also shows that HVJ-E induces IL-12 and IL-6 of dendritic cells (paragraph [0282], Fig. 18), and Example 6 shows that HVJ-E inhibits regulatory T cell (paragraph [0285], Fig. 20). In light of such descriptions, the specification clearly describes the methods of claims 69, 92-94 in such a way as to enable one skilled in the art to carry out the claimed methods.

Second, there is no scientific basis for the assertion that one of skill in the art would not expect an immune adjuvant to have an anti-tumor effect in the absence of a chemotherapeutic agent. General anti-tumor immunity—more specifically, immune responses stimulated by a tumor cell antigen—is well known. Stimulation of the immune response induces the immune system to attack tumor cells, which in turn, provokes cell death or inhibition of cell proliferation, thereby providing an anti-tumor effect. See Khanna (*Immunol. Cell Biol. 76*, 20-26, 1998): "The concept

of a role for the immune system in the control and elimination of malignant cells has existed for many years, giving rise to the theory of immunological surveillance against tumors" (beginning of Introduction) and ". . . tumor cells can present tumor-associated epitopes (TAE) on their surface in conjunction with MHC molecules which can be recognized by CTL" (Introduction, lines 7-10). Boura (Hepato-Gastroenterology, Vol.48, 10404044, 2001) also describes, "There is now ample evidence that T cell responses exist in several human cancers" (pp.1040, left column, lines 8-9) and "[t]he concept of tumor surveillance by the immune system implies that cellular immune responses are elicited against tumor cells by circulating T cells, activated macrophages, NK cells and lymphokine-activated killer cells (LAK cells)" (pp. 1040, right column, lines 20-24). From these descriptions, it is clear that a protein which is expressed on the surface of a cancer cell can induce a cellular immune response against cancer. Thus, those of skill in the art reading the present specification, including its working examples, would accept the specification's teaching that an HVJ-E can enhance anti-tumor immunity as an immune adjuvant whether or not it is combined with a chemotherapeutic agent.

The Examiner's failure to articulate a reasonable basis for challenging the enablement of the rejected claims alone is fatal to this rejection and is not sufficient to shift the burden to the Applicants. Nevertheless, to advance prosecution, Applicants include with this response three post-filing date references and a Declaration under 37 C.F.R. § 1.132 of Toshihiro NAKAJIMA. The post-filing date references demonstrate that administration of an HVJ-E alone has an anti-tumor effect against colon cancer (see Fig. 1 of Kurooka & Kaneda, *Cancer Res. 67*, 227-236, 2007; provided with the accompanying IDS), Renca renal cell carcinoma (see Fig.4a of Fujihara *et al.*, *Cancer Immunol. Immunother. 57*, 73-84, 2008; provided with the accompanying IDS), and prostate cancer (see Fig. 6 of Kawaguchi *et al.*, *Int. J. Cancer 124*, 2478-87, 2009; provided with the accompanying IDS). The Declaration provides evidence that intratumoral injections of

HVJ-E—in the absence of a chemotherapeutic compound—results in a significant level of tumor growth inhibition and prolongation of survival in a mouse melanoma model. As the Declaration explains, these data indicate the potential of HVJ-E as a new therapeutic agent for melanoma.

There is no scientific or legal basis to support the assertion that claims 69 and 92-94 are not enabled. In fact, the evidence of record demonstrates that the specification does enable the claimed methods. Please withdraw the rejection.

Previous Rejection Over Kaneda, EP1170363

Claims 69 and 92 previously were rejected under 35 U.S.C. § 102(b) as anticipated by Kaneda, EP1170363. The Office Action notes that this rejection may be reinstated in the next Office Action if the rejection under 35 U.S.C. § 112 ¶ 1 is overcome. There is no basis for rejecting claims 69 and 92 over EP1170363.

First, "gene transfer vector," "gene vector," and "virus envelope vector" as disclosed in EP1170363 refers to a vector obtained by encapsulating an exogenous gene in a virus vector envelope; see paragraph [0033]. The EP1170363 invention relates to the use of HVJ-E as a "gene transfer vector" which encloses an exogenous gene. In contrast, as indicated in the Examples, the HVJ-E of the present invention is an envelope obtained by inactivating an endogenous gene in the HVJ and does not contain a foreign gene; it is therefore structurally different than the gene transfer vector disclosed in EP1170363.

Second, EP1170363 does not teach a method for inhibiting tumor cell growth by administering an effective amount of a composition consisting essentially of HVJ-E as recited in claims 69 and 92. This conclusion is supported by the publication of Kurooka & Kaneda, cited above, which was published after the 2001 filing date of EP1170363. The authors, Masayuki Kurooka and Yasufumi Kaneda, assert that theirs "is the first report to show that HVJ-E alone can

eradicate tumors . . . ." (abstract). Yasufumi Kaneda is one of the two inventors named on the EP1170363 application. This statement, made in apparent ignorance of the present application, indicates that one of the EP1170363 inventors himself did not understand EP1170363 to disclose a method of using HVJ-E alone to treat tumors.

Respectfully submitted,

BANNER & WITCOFF, LTD.

/Lisa M. Hemmendinger/

Date: January 27, 2010 By: _____

Lisa M. Hemmendinger
Registration No. 42,653

Customer No. 22907
202-824-3000